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COLIFORM INFECTION OF THE URINARY TRACT

BY

P. N. COLEMAN AND S. TAYLOR

From the Laboratory, Townleys Hospital, Bolton, Lancashire

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This paper concerns the investigation of the types of coliform organisms encountered in the urines of one hundred consecutive cases of pyuria admitted to Townleys Hospital, Bolton, during 1948. Recently Warner (1948), discussing urinary infection in paraplegic patients, has drawn attention to the frequency with which *Bact. aerogenes* was found. This organism was insensitive both to sulphanilamide and to penicillin, and Warner considered that these drugs may be of only limited value in urinary infection. It was thought that it would be interesting to discover if a similar high incidence of *Bact. aerogenes* would be found in other types of urinary infection and to consider all the types of coliform organisms found from the point of view of chemotherapy.

Methods

Wet and stained films of centrifuged deposits from catheter specimens of the urines were examined and the urines cultured on MacConkey's medium and blood agar. Any coliform bacilli isolated were identified by biochemical tests, and their sensitivity to sulphanilamide, penicillin, and streptomycin was determined. The fermentation reactions using glucose, mannitol, lactose, sucrose, and salicin were employed. Other tests used were: the formation of indole, gas production at 44° C., utilization of citrate, Vosges Proskauer test (Barritt's modification), and the methyl red reaction. The coliform bacilli were identified by the criteria described in Topley and Wilson's *Principles of Bacteriology and Immunity* (third edition).

Of the eighteen strains of *Bact. aerogenes* tested, six produced gas at 44° C. after 48 hours' incubation though not after 24 hours'. They were, however, classified as *Bact. aerogenes*. *P. vulgaris* was distinguished from *P. morgani* by the ability to swarm on blood agar. The paracolon bacilli included three anaerogenic strains, two of which were late lactose fermenters.

Sulphanilamide sensitivity tests were carried out by the method of Harper and Cawston (1945). Penicillin and streptomycin sensitivities were determined by inoculating one drop of an overnight broth culture of the organism under test into broth containing the drug in the appropriate concentration. These cultures were incubated overnight and examined for growth next morning.

Results

Table I shows the incidence of the varieties of coliform and other organisms associated with various clinical conditions. The cases were divided into two groups: group 1, in which there was no gross lesion of the urinary tract; and group 2, where infection was secondary to a surgical or medical condition affecting the tract.

It was found that in group 1 *Bact. coli* was the predominant organism (49 strains compared with 12 of other organisms) whereas in group 2 *Bact. coli* was relatively uncommon (7 strains compared with 56 of other organisms). Its place was taken in roughly equal proportions by *P. vulgaris, P. morgani,* and *Bact. aerogenes.* In group 1 pure cultures were frequent and Gram-positive cocci infrequent; in group 2 the reverse was found.

Table II shows the sensitivities to sulphanilamide, penicillin, and streptomycin. In planning these tests regard was paid to the concentrations that could be obtained in the urine. The Medical Research Council pamphlet suggests that concentration of sulphanilamide of 100 mg./100 ml. of urine can readily be obtained. Peeney (1946) found that concentrations of up to 200 units per ml. of penicillin could be maintained in the urine, while Petroff and Lucas (1947) obtained average concentration of 70 to 100 μg. of streptomycin per ml. Table II shows that bacteriostatic concentration to *Bact. coli* can be obtained in the urine both by sulphanilamide and by penicillin, to *P. vulgaris* by penicillin, and to a few strains (4 out of 19) by sulphanilamide. Bacteriostatic concentrations could not be obtained with either of these two drugs against *Bact. aerogenes* or *P. morgani.* All but one of the coliform strains tested were sensitive to streptomycin.

TABLE I

VARIETIES OF COLIFORM AND OTHER ORGANISMS ASSOCIATED WITH VARIOUS CLINICAL CONDITIONS

		No. of cases	*Bact. coli*	*Bact. aerogenes*	*P. vulgaris*	*P. morgani*	Atypical *Bact. coli*	Paracolon bacilli	*Ps. pyocyanea*	*Bact. alkaligenes*	Gram-positive cocci	Pure culture
Group 1: Cases without gross lesion of urinary tract	Acute pyelitis with fever and pain:											
	(*a*) pregnancy	16	16	—	—	—	—	—	—	—	—	16
	(*b*) non-pregnant	5	5	—	—	—	—	—	—	—	—	5
	Pyelitis of pregnancy without fever or pain ..	11	10	1	—	—	—	—	—	—	—	11
	Pyelitis in children	2	1	—	—	—	1	—	—	—	—	2
	Cystitis of pregnancy	7	2	—	1	—	2	3	—	—	2	4
	Cystitis of puerperium ..	8	8	—	—	—	—	—	—	—	4	4
	Cystitis ..	11	7	—	2	—	—	1	—	1	5	6
	Total, Group 1	60	49	1	3	—	3	4	—	1	11	48
Group 2: Cases with surgical or medical lesion affecting the urinary tract	Enlargement of prostate ..	29	4	14	14	13	—	2	3	—	23	5
	Paraplegia ..	7	3	2	2	1	—	—	—	—	5	1
	Papilloma of bladder ..	2	—	1	—	—	1	—	—	—	1	1
	Extravasation of urine	1	—	1	—	—	—	—	—	—	—	1
	Vesicovaginal fistula	1	—	—	1	—	1	—	—	—	1	—
	Total, Group 2	40	7	18	17	14	2	2	3	—	30	8

In group 2 there were two females and in group 1 three males: two young men with acute pyelitis and one child with pyelitis.

TABLE II

CONCENTRATION OF DRUG TO WHICH ORGANISMS ARE SENSITIVE

	Penicillin units per ml.				Sulphanilamide mg. per 100 ml.					Streptomycin μg. per ml.						
	No. of strains tested	Not sensitive >500	500 to 100	Less than 100	No. of strains tested	Not sensitive >200	200 to 100	100 to 20	Less than 20	No. of strains tested	1,000 to 500	100 to 50	50 to 25	25 to 10	10 to 5	5 to 2.5	Less than 2.5
Bact. coli	56	1	2	53	56	1	2	22	31	27	—	—	—	2	8	15	2
Bact. aerogenes ..	19	19	—	—	19	17	—	2	—	12	—	—	—	—	1	7	4
Proteus vulgaris ..	20	—	—	20	19	15	—	1	3	16	—	1	15	—	—	—	—
P. morgani	14	13	1	—	12	11	—	1	—	10	1	—	2	1	1	5	—
Atypical *Bact. coli*	5	1	2	2	5	—	—	4	1	4	—	—	—	—	—	4	—
Ps. pyocyanea	3	3	—	—	3	3	—	—	—	3	—	—	—	2	1	—	—
Paracolon bacilli ..	6	1	3	2	6	—	1	4	1	3	—	—	—	1	—	1	1
Bact. alkaligenes ..	1	—	—	1	1	—	—	—	1	1	—	—	—	—	—	—	1

A number of sensitive organisms were tested at concentrations of penicillin 50 units/ml. Out of 31 strains of *Bact. coli* tested 23 strains showed a good growth, 6 strains showed some inhibition, and 2 strains were completely inhibited. Out of 14 strains of *P. vulgaris* tested, 4 gave a good growth in 50 units/ml. penicillin, 8 showed some inhibition, and 2 were completely inhibited.

Discussion

Reports vary of the incidence of the different types of coliform bacilli in urinary infections. Thus in 200 cultures from all clinical types of infection Hill *et al.* (1929) found 100 strains of *Bact. coli*, 79 strains of *Bact. aerogenes*, and 5 strains of the proteus group. In the urine of paraplegic patients Petroff and Lucas (1946) found 41% of the coliform organisms were *Bact. aerogenes* and 16% proteus, while Warner (1948), considering only those which fermented lactose, found 32 out of 50 coliform organisms studied were *Bact. aerogenes*. On the other hand, Cross (1937), in a series from which urinary infections secondary to prostatic enlargement were excluded, found 17 strains of *Bact. coli*, 2 of *Bact. aerogenes*, and 5 of other organisms. Marple (1941) in a series of thirteen cases of women with pyuria found *Bact. coli* strains only, and Dodds (1931), considering urinary infection in pregnancy, found 49 *Bact. coli* strains and only one *Bact. aerogenes* (*Bact. friedlander*).

The present findings suggest that the rate of urinary flow may be the factor which determines the incidence of *Bact. coli* in infected urines. In this series the group of cases of primary urinary infection consists largely of women and includes a high proportion of cases occurring in pregnancy, whereas the group of cases of infections secondary to obstruction includes a large proportion of cases with enlargement of the prostate. No doubt this distribution of cases is determined in part by the type of case admitted to the particular hospital, but it is thought that any representative series of cases of urinary infection would show that the primary cases were much commoner in women than in men, that in women they were often associated with pregnancy, and that the commonest cause of urinary obstruction was enlargement of the prostate (and for this reason the group where the infection was secondary to obstruction would include many cases of this condition). The series is considered, therefore, representative enough to draw general conclusions.

A possible explanation of the difference in distribution of *Bact. coli* infections between the two groups might be that in the first group the pyuria represents infection of kidney or bladder tissue, the urine in these cases flowing too freely to admit much bacteriological multiplication, whereas in the second group stagnation of the urine is the important factor and growth of bacteria occurs in the urine itself. As a tissue invader *Bact. coli* might be the most successful organism, whereas for growth in the poor medium afforded by stagnant urine the saprophytic organisms *Bact. aerogenes*, *P. vulgaris*, and *P. morgani* might have the advantage.

The results of the sensitivity tests compare with the findings of previous papers. *Bact. coli* is sensitive to sulphanilamide (Strauss and Finland, 1941; M.R.C. pamphlet on sulphonamides, 1943), while *Bact. aerogenes* (Warner, 1948), *P. vulgaris* (M.R.C. pamphlet; Stewart, 1945), and *P. morgani* (Neter and Clark, 1944) are relatively non-sensitive. *Bact. coli* and *P. vulgaris* are relatively sensitive to penicillin (Warner, 1948; Stewart, 1945; Peeney, 1947), *Bact. aerogenes* and *P. morgani* are not (Warner, 1948; Helmholz and Sung, 1944; Peeney, 1947). On the other hand, Warner found that the 12 *Bact. coli* strains tested as well as the *Bact. aerogenes* strains were insensitive to 50 mg./100 ml. of sulphathiazole.

Comparing the results of the sensitivity tests with the incidence of the various types of coliform organisms investigated, success in the treatment with sulphanilamide might be expected in the non-obstructive cases since *Bact. coli* is the commonest infecting organism, but not in the cases secondary to obstruction because coliform organisms which are not sensitive predominate in this type of infection. The use of penicillin might improve results in the cases of urinary obstruction because of its additional action on *P. vulgaris*. In the present series, however, although *P. vulgaris* was found in the urine of seventeen out of forty cases of infection secondary to obstruction, in twelve of these cases it was accompanied by *Bact. aerogenes* or *P. morgani*, organisms insensitive to penicillin. In cases of urinary obstruction there is the additional factor that while the obstruction is unrelieved there is a continuing liability to reinfection; but even if this factor is disregarded the series shows the prospects for chemotherapy by sulphanilamide and penicillin are not good.

These findings are in accord with clinical experience. Thus Brown (1946), discussing the treatment of the urinary infections of pregnancy with sulphanilamide, states the results are very satisfactory; and Donovan (1947) found that sulphonamides would not sterilize the urines of his paraplegic patients.

Streptomycin, when it becomes available, would seem to offer for the first time the possibility of obtaining a bacteriostatic concentration effective against all types of coliform bacilli found in urinary obstruction. However, the liability to reinfection on withdrawal of the drug remains, and reports emphasize the rapid development of insensitive strains. Perhaps the most useful func-

tion of streptomycin will prove to be the obtaining of a sterile field for a limited period during which a surgical operation for relief of obstruction can be carried out.

Summary

1. The incidence of different types of coliform bacilli in cases of urinary infection has been studied. A comparison has been made between types isolated from cases of primary urinary infection and urinary obstruction. Sensitivities to sulphanilamides, penicillin, and streptomycin were determined.

2. In cases of primary urinary infection *Bact. coli* was the predominant organism; in cases secondary to urinary obstruction *Bact. aerogenes*, *P. vulgaris*, and *P. morgani* predominated.

3. *Bact. coli* is sensitive to sulphanilamide and penicillin in concentration obtainable in urine. *P. vulgaris* is sensitive to penicillin, but *P. morgani* and *Bact aerogenes* are sensitive to neither of these drugs. All types of coliform bacilli tested are sensitive to streptomycin.

4. Because of the high incidence of non-sensitive strains found in cases of urinary infection secondary to obstruction, no benefit from treatment with sulphonamides or penicillin is likely.

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